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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,610	07/23/2001	Hagit Amitai	AMITAI 1	2065

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EXAMINER	
LI, RUIXIANG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 01/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/807,610	AMITAI ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears n the cover she t with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,7,9-14 and 16* is/are pending in the application.

4a) Of the above claim(s) *13 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,7,9-12 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of Application

The Request filed on October 23, 2003 for Continued Examination (RCE) under 37 CFR 1.114 of Application 09/735,712 is granted. An action on the RCE follows.

Applicants' Amendment

Applicants' amendment filed on October 27, 2003 has been entered in full. Claims 2, 4, 6, 8, and 15 have been canceled. Claims 1, 9, and 16 have been amended. Claims 1, 3, 5, 7, 9-14, and 16 are pending. Claims 1, 3, 5, 7, 9-12, and 16 are under consideration, whereas claims 13 and 14 are withdrawn from consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Withdrawn Rejections

The rejection of claims 9-12 and 16 under 35 U.S.C. §101, as set forth in the previous Office Action (Paper No. 14 and 16), has been withdrawn in view of Applicants' amendment to the claims.

The rejection of claims 1-8 under 35 U.S.C. § 103(a), as set forth in previous Office Action (Paper No. 14 and paper No. 16), has been withdrawn in view of applicants' cancellation of claims 2, 4, 6, and 8, and amendment to claim 1.

Claim Rejections Under 35 U. S. C. § 112, 2nd Paragraph

(i) The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(ii) Claims 1, 3, 5, 7, 9-12, and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it recites "a DNA segment encoding a genomic growth hormone signal peptide with an intron". It is unclear how a genomic growth hormone signal peptide differs from a growth hormone signal peptide generally referred in the art and whether the term "with an intron" modifies the DNA segment or the signal peptide. Applicants may intend to refer to an expression vector comprising a growth hormone signal peptide genomic DNA sequence. However, the claim, as written, is confusing, rendering the claim indefinite. Claims 3, 5, 7, 9-12, and 16 depend, either directly or indirectly, from claim 1.

Claim Rejections Under 35 U. S. C. § 103(a)

(i) The rejection of claims 9-12 and 16 under 35 U.S.C. § 103(a) as being unpatentable over Pecceu et al. (Gene, 97:253-258, 1991) and Bjorkdahl et al. (Cancer Immunol. Immunother. 44:273-281, 1997) in view of Muzio et al. (WO 9612022, April 25, 1996), as set forth in previous Office Action (Paper No. 14 and paper No. 16), remains.

Applicants' amendment to claim 1 fails to limit the isolated glycosylated icIL-1ra-II claimed in claim 9, which recites a product by process. It is noted that a product is a product regardless of how it is made. Claims 10-12 depend upon claims 9. In addition, amended claim 16 is drawn to an isolated glycosylated icIL-1ra-II. Since the expression of the fusion protein comprising the signal peptide of human growth hormone and icIL-1ra-II taught by Pecceu et al. and Bjorkdahl et al. in combination with Muzio et al. would necessarily produce a glycosylated icIL-1ra-II, the claims remain rejected.

(ii) Claims 1, 3, 5, 7, 9-12, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pecceu et al. (*IDS*, Gene, 97:253-258, 1991) and Selden et al. (U.S. Patent NO. 6,083,725, date of patent: July 4, 2000; earliest priority date: September 13, 1996) in view of Muzio et al. (*IDS*, WO 9612022, April 25, 1996).

Pecceu et al. teach an expression vector, pSV1003, comprising a DNA segment encoding the signal peptide of human growth hormone and a DNA segment ecoding the mature form of interleukin-1β (IL-1β). The expression of this fusion protein in Chinese hamster ovary cells results in virtually complete secretion of a glycosylated form of IL-

1β, which was recovered (See legend to Fig. 3) and shown to be biologically active (See, e.g., right volumn of page 257, under conclusions). The results suggest that fusion of mature IL-1β to a heterologous signal peptide allowed the protein to cross the membrane of the rough endoplasmic reticulum and to follow the pathway of a typical secretory protein. Transport of IL-1β to ER and Golgi apparatus after signal cleavage allowed full glycosylation (bottom of left column to top of right column of page 257).

Selden et al. teach an expression construct comprising a human growth hormone signal peptide genomic DNA sequence either with an intron (SEQ ID NO: 27) or without the intron (SEQ ID NO: 22) and human α-gal A cDNA, and expression of the secreted α-gal A enzyme in human cells (see. e.g., Example I; claims 1, 3, 4, and 7).

Neither Pecceu et al. nor Selden et al. teach expression of a fusion protein comprising interleukin-1 receptor antagonist type II (icIL-1ra-II).

Muzio et al. teach intracellular expression of icIL-1ra-II in COS cells (see, e.g., page 10), which is naturally expressed in different cells, including human PMN, monocytes, and fibroblasts (Fig. 2). Muzio et al. also teach a method for producing the recombinant icIL-1ra-II (see, e.g., claim 10). The recombinant icIL-1ra-II showed a mass of approximately 25 KDa (line of 21 of page 10) by Western blot analysis on SDS gel (Fig. 3). Muzio et al. further teach a pharmaceutical composition comprising icIL-1ra-II (top of page 3 and 6th paragraph of page 5).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to construct a fusion protein comprising a signal peptide of a protein which is normally expressed and secreted by human cells, such as

the signal peptide of human growth hormone (encoded by either a cDNA sequence or a genomic DEA sequence withan intron) as taught by Pecceu et al. and Selden et al, and the interleukin-1 receptor antagonist type II as taught by Muzio et al. to express and to produce the secreted icIL-1ra-II in a host cell, including an isolated human cell, with a reasonable expectation of success. One would have been motivated to do so because (i) it is routine for one skilled in the art to produce a secretory protein by fusion of a non-secretory protein with a signal peptide of another secretory protein, as exemplified by Pecceu et al. and Selden et al; and (ii) icIL-1ra-II is an active interleukin-1 receptor antagonist and has important biological activity as demonstrated by Muzio et al. (See, e.g., Fig. 4).

It is noted that the intended use recited in claim 1, "to produce an icIL-1ra-II where the amino acid sequence at the N-terminus is SEQ ID NO: 11", does not limit the instant product claim. In addition, an expression construct comprising a human growth hormone signal peptide genomic DNA sequence with an intron (SEQ ID NO: 27) would necessarily produce the recited claimed icIL-1ra-II, which would have an apparent molecular weight of about 27 or 30 KDa on SDS-PAGE under reducing conditions with 15% acrylamide.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (703) 306-0282. The examiner can normally be reached on Monday-Friday, 8:30 am-5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Ruixiang Li
Examiner
December 24, 2003

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600